IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (withdrawn) A polynucleotide which comprises the base sequence of SEQ ID NO: 1 and includes a promoter region of DR3 gene associated with RA, wherein the base sequence from base 170 to 175 of the polynucleotide constitutes a TCCTCC motif that is associated with transcription activity, and wherein allele-specific methylation occurs in some of CpG sequences that occur subsequent to the TCCTCC motif.

2. (withdrawn) A polynucleotide as set forth in Claim 1, wherein allele-specific methylation occurs in CpG sequences located from –380 bp to –180 bp relative to a translation initiation point of the DR3 gene.

3. (withdrawn) A polynucleotide as set forth in Claim 1, wherein allele-specific methylation occurs in CpG sequences located from –380 bp to –180 bp relative to a translation initiation point of the DR3 gene, and wherein CpG sequences downstream to –180 bp are either methylated or unmethylated.

4. (withdrawn) A determining kit for determining development of RA or the likelihood of developing RA, wherein a comparison is made in regard to methylation state between a DR3 gene promoter region obtained from synovial cells or synovial infiltrating lymphocytes and a DR3 gene promoter region obtained from peripheral blood lymphocytes,

said kit comprising methylation-specific primers and unmethylation-specific primers, which are used to determine the presence or absence of methylated cytosines in at least part of a polynucleotide constituting the DR3 gene promoter region.

5. (withdrawn) A determining kit as set forth in Claim 4, wherein the methylation-specific primers and the unmethylation-specific primers are designed to amplify at least the base sequence from base 374 to 564 of the base sequence set forth in SEQ ID NO: 1.

6. (withdrawn) A determining kit as set forth in Claim 4, wherein the kit determines that the subject has developed RA or has the likelihood of developing RA when the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is more strongly methylated than the DR3 gene promoter region obtained from the peripheral blood lymphocytes, or when the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is confirmed to be strongly methylated.

7. (original) A method for determining development of RA or the likelihood of developing RA, comprising: comparing a methylation state of a DR3 gene promoter region obtained from synovial cells or synovial infiltrating lymphocytes with a methylation state of a DR3 gene promoter region obtained from peripheral blood lymphocytes, or confirming that the DR3 gene promoter region obtained from the synovial cells is strongly methylated.

8. (original) A method as set forth in Claim 7, further comprising:

a DNA converting step of converting unmethylated cytosines to uracils in CpG sequences contained in the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes, and the DR3 gene promoter region obtained from the peripheral blood lymphocytes, by treating the respective DR3 gene promoter regions with a bisulfite-containing reagent;

a DNA amplifying step of amplifying the DR3 gene promoter regions, after the treatment in the DNA converting step, by a polymerase chain reaction using methylation-specific primers or unmethylation-specific primers;

a methylation-state detecting step of detecting a methylation state of the DR3 gene promoter regions by detecting whether the polymerase chain reaction in the DNA amplifying step using the methylation-specific primers or the unmethylation-specific primers has amplified the DR3 gene promoter regions; and

a comparing step of comparing the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes with the DR3 gene promoter region obtained from the peripheral blood lymphocytes, in regard to the methylation state of the DR3 gene promoter A regions detected in the methylation-state detecting step, or a confirming step of confirming that the DR3 promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is strongly methylated.

9. (previously presented) A method as set forth in Claim 7, wherein the method determines that the subject has developed RA or has the likelihood of developing RA when the DR3 promoter region obtained from the synovial cells or synovial infiltrating

lymphocytes is more strongly methylated than the DR3 promoter region obtained from the peripheral blood lymphocytes.

10. (previously presented) A method as set forth in Claim 7,

wherein a DR3 gene originating in the peripheral blood lymphocytes of healthy subjects is used as a control; and

wherein the method determines that the subject has developed RA or has the likelihood of developing RA when the DR3 gene promoter region obtained from the synovial cells or synovial infiltrating lymphocytes is more strongly methylated than the DR3 promoter region originating in the peripheral blood lymphocytes.

Claims 11-12 (canceled)